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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/577,084	05/24/2000	Keiya Ozawa	50026/012002	5150
21559	7590	07/27/2004	EXAMINER	
CLARK & ELBING LLP 101 FEDERAL STREET BOSTON, MA 02110			KAPUST, RACHEL B	
			ART UNIT	PAPER NUMBER
			1647	

DATE MAILED: 07/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/577,084

Applicant(s)

OZAWA ET AL.

Examiner

Rachel B. Kapust

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4-10,12 and 14-24 is/are pending in the application.
- 4a) Of the above claim(s) 9 and 19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4-8,10,12,14-18, 20, and 23-24 is/are rejected.
- 7) ☒ Claim(s) 21 and 22 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 May 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 0204, 0604, 0404.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

RESPONSE TO AMENDMENT

Applicant's amendment filed May 4, 2004 is acknowledged. Claims 3, 11, and 13 have been canceled. Claims 1, 2, 4, 5, 7, 10, 12, 14, and 15 are amended. Claims 21-24 are new. Claims 1, 2, 4-8, 10, 12, 14-18, and 20-24 are under consideration. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claim Rejections/Objections Withdrawn

The objection to the specification for incorrect character spacing on p. 4 is withdrawn in response to Applicants' amendment to the specification.

The rejection of claims 1, 2, 4-8, 10, 12, 14-18, and 20 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in response to Applicants' amendment to claim 1. The rejection of claims 3, 11, and 13 is withdrawn in response to Applicants' cancellation of these claims.

The rejection of claims 2 and 12 under 35 U.S.C. 112, first paragraph, for lack of enablement is withdrawn in response to Applicants' amendments to claims 1, 2, 10, and 12. The rejection of claims 3, 11, and 13 is withdrawn in response to Applicants' cancellation of these claims.

The rejection of claims 2 and 12 under 35 U.S.C. 112, first paragraph, for failing to comply with the written description requirement is withdrawn in response to Applicants' amendments to claims 1, 2, 10, and 12. The rejection of claims 3, 11, and 13 is withdrawn in response to Applicants' cancellation of these claims.

The rejection of claims 1-2, 6-8, and 20 under 35 U.S.C. 102(b) as being anticipated by Gurney *et al.* is withdrawn, because the claims, as amended, are no longer anticipated by Gurney *et al.* The rejection of claim 3 is withdrawn in response to Applicants' cancellation of the claim.

The rejection of claims 1, 6-8, and 20 under 35 U.S.C. 102(b) as being anticipated by Maruyama *et al.* is withdrawn, because the claims, as amended, are no longer anticipated by Maruyama *et al.* Maruyama *et al.* do not teach a fusion protein comprising a ligand binding domain of a steroid hormone receptor.

Claim Rejections - 35 USC § 112

The rejection of claims 1, 4-8, 10, 14-18, and 20 under 35 U.S.C. 112, first paragraph, for lack of enablement is maintained for reasons of record on p. 4-5 of the office action of paper no. 21. Claims 23-24 are newly rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for chimeric proteins comprising a ligand binding domain of a steroid hormone receptor and c-mpl, does not reasonably provide enablement for chimeric proteins comprising any cytokine receptor or any part of a cytokine receptor that imparts proliferation activity to a cell.

Applicants argue that the specification provides examples of cytokine receptors such as c-mpl, c-kit, and flk2/flt3 (p. 17 of response). Applicants argue that the disclosed exemplary c-mpl receptor is representative of cytokine receptors, and one skilled in the art would recognize that Applicants' claimed fusion protein invention encompassed a variety of cytokine receptors (p. 18 of response). Applicants further argue that "those skilled in the art routinely screen many fusion proteins in order to isolate a fusion protein having the desired effect; such screening is routine in the art and does not constitute undue experimentation" (p. 18 of response). Applicants also argue that it is not necessary for all possible embodiments of a claim to be operative in order for that claim to be enabled, and that the proper test of enablement is whether one reasonably skilled in the art could make and use the claimed invention from the disclosure in the patent coupled with information known in the art without undue experimentation (p. 20 of response).

Applicants' arguments have been fully considered but have not been found to be persuasive. It is true that one skilled in the art would recognize that Applicants' claimed fusion protein encompasses a variety of cytokine receptors. However, as stated in the office action of paper no. 21, the ability of cytokine receptors to induce cell proliferation is not a universal

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feature of all cytokine receptors. The receptors for the various cytokines are quite diverse structurally, and they belong to five families of receptor proteins: immunoglobulin superfamily receptors, class I cytokine receptor family (hematopoietin receptor family), class II cytokine receptor family (interferon receptor family), TNF receptor family, and chemokine receptor family (see, for example, Kuby, J. (1997), Immunology 3rd Edition, W.H. Freeman and Company, p. 321). As written, the claims encompass any cytokine receptor from any of the aforementioned cytokine receptor families. This is not merely a situation where certain embodiments are inoperative, and a skilled artisan would know not to try certain cytokine receptors. Here, the claims encompass entire families of cytokine receptors that would not be predictably useful. This is a situation in which one of skill in the art would need to first engineer a fusion protein and test its function before knowing whether or not the cytokine receptor imparts a proliferation activity to a cell. In addition, one of skill in the art would need to perform experiments like that of Gurney *et al.* in order to determine what region of the cytokine receptor is sufficient for inducing cell proliferation. Although the methods used in engineering fusion proteins and screening them for activity are routine in the art, the quantity of experimentation necessary for determining what portions of cytokine receptors impart proliferation and which cytokine receptors are able to induce proliferation is undue.

The rejection of claims 1, 4-8, 10, 14-18, and 20 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained for reasons of record on p. 6 of the office action of paper no. 21. Claims 23-24 are newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Applicants argue that the specification conveys that the inventors possessed the presently claimed invention, because the specification teaches that “any cytokine receptor can also be used in the present invention as long as it imparts proliferation activity to a cell upon association” (p. 12 of response). Applicants also point to the exemplary fusion proteins described in Figure 20 and in Example 8 of the specification. Applicants further argue that the disclosed exemplary c-mpl receptor is representative of cytokine receptors, because no substantial variation exists with

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respect to proliferation-inducing domains within the family of cytokine receptors (p. 15 of response).

Applicants' arguments have been fully considered but have not been found to be persuasive. Although the specification teaches that any cytokine receptor may be used so long as it imparts proliferation activity to a cell, such a claim is not equivalent to evidence that Applicants were either in possession of the encompassed fusion proteins at the time the application was filed or that one of skill in the art could visualize or recognize the full scope of the biological materials claimed. As stated above, there is substantial structural diversity amongst the different families of cytokine receptors, and proteins classified as cytokine receptors are not predictably activated by dimerization, nor do they predictably induce proliferation.

In order to visualize or recognize the full scope of the biological materials claimed, a person having ordinary skill in the art is required to perform one or more tasks, utilize one or more skills, to determine the complete identity of those biological materials reasonably expected to perform the functions the claims require, obtain those materials, and confirm their expectations for those materials. Only after persons skilled in the art prepare new DNA and test that DNA for fusion protein functionality will they know whether Applicants would have the right to exclude them from making and using the new DNA constructs that they prepared. Therefore, the specification does not provide an adequate written description of the subject matter claimed.

Claim Rejections - 35 USC § 103

The rejection of claim 4 under 35 U.S.C. 103(a) as being unpatentable over Gurney *et al.* in view of Wang *et al.* is maintained for reasons of record on p. 8 of the office action of paper no. 21. Claims 1, 2, 4, 6-8, 20, and 23 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Gurney *et al.* in view of Wang *et al.*

Applicants argue that one of ordinary skill in the art would not be motivated to combine the ligand binding domain of a steroid hormone receptor with a cytokine receptor. Applicants further argue that "Gurney describes combining two cytokine receptors and Wang describes the combination of two intranuclear proteins...thus, both references merely describe combinations of

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proteins that are similar to each other" (p. 24 of response). Applicants argue that the art teaches that if two similar proteins are used to produce a fusion protein, homodimerization may occur. Applicants argue that in contrast, the present claims are directed to "the inventive concept of creating a fusion protein including two different types of polypeptides" (p. 24 of response). In addition, Applicants argue that in view of the scope of enablement rejection of the claims, one skilled in the art would not have readily exchanged the growth hormone receptor portion for an estrogen receptor portion (p. 26 of the response).

Applicants' arguments have been fully considered but have not been found to be persuasive. Gurney *et al.* did not combine two cytokine receptors merely because they are similar to each other. Rather, Gurney *et al.* used the growth hormone receptor (GHR) in the fusion protein because GHR "is one of the best characterized members of the cytokine receptor family" and "GH (growth hormone) induces homodimerization of the receptor" (p. 5296, column 1). In order to characterize the proliferation activity of the intracellular domain of c-mpl, which must be in the dimer form in order for it to be active, Gurney *et al.* engineered the GHR-c-mpl fusion protein so that dimerization of c-mpl could be induced by GH. Also, the rejection is not in conflict with the scope of enablement rejection, because the claims were originally drawn to any ligand-binding domain, and it is not known whether all ligand-binding domains form homodimers. Wang *et al.*, however, teach that estrogen receptors form homodimers upon binding to estradiol-17B, tamoxifen, or ICI 182,780. It would have been obvious to one of ordinary skill in the art to fuse c-mpl to any ligand-binding domain that forms homodimers in order to study the proliferation activity of c-mpl.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1, 4, and 23 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1 and 3 of copending Application No. 09/142305. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented. Claim 1 is drawn to a fusion protein comprising (a) a first polypeptide which comprises a ligand binding domain of a steroid hormone receptor that upon ligand-binding dimerizes and (b) a second polypeptide which comprises a cytokine receptor or a proliferation-inducing part thereof that imparts proliferation activity to a cell after the steroid hormone receptor dimerizes. Claim 4 is drawn to the fusion protein of claim 1 wherein the steroid hormone receptor is an estrogen receptor. Claim 23 is drawn to the fusion protein of claim 1 wherein the steroid hormone receptor is an estrogen receptor, androgen receptor, progesterone receptor, glucocorticoid receptor or mineral corticoid receptor.

Claim 1 of App. No. 09/142305 is drawn to a fusion protein comprising (a) a steroid hormone receptor that dimerizes once a ligand binds to the ligand-binding domain of the steroid hormone receptor and (b) a cytokine receptor or part thereof that imparts proliferation activity to a cell upon the dimerization of the steroid hormone receptor. Claim 3 of App. No. 09/142305 is drawn to the fusion protein of claim 1 wherein the steroid hormone receptor is an estrogen receptor, androgen receptor, progesterone receptor, glucocorticoid receptor or mineral corticoid receptor. Thus, claims 1, 4, and 23 of the current application are drawn to the same inventions as that of claims 1 and 3 of App. No. 09/142305.

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Conclusion

Claims 21 and 22 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 1, 2, 4-8, 10, 12, 14-18, 20, 23, and 24 are rejected. Claims 21 and 22 are objected to.

The following articles, patents, and published patent applications were found by the Examiner during the art search while not relied upon are considered pertinent to the instant application:

Vigon *et al.* (1993), *Oncogene* 8(10): 2607-2615

Skoda *et al.* (1993), *EMBO J* 12(7): 2645-2653


Baumann *et al.* (1994), *J Biol Chem* 269(23): 16297-16304

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rachel B. Kapust whose telephone number is (571) 272-0886. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RBK
7/26/04


JANET ANDRES
PRIMARY EXAMINER